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(12) **United States Patent**  
**Krishna et al.**(10) **Patent No.:** US 7,582,727 B1  
(45) **Date of Patent:** \*Sep. 1, 2009(54) **PHARMACEUTICAL FORMULATIONS OF BIVALIRUDIN AND PROCESSES OF MAKING THE SAME**2008/0051558 A1 2/2008 Zhou  
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2009/0062511 A1 3/2009 Palle et al.(75) Inventors: **Gopal Krishna**, Parsippany, NJ (US);  
**Gary Musso**, Parsippany, NJ (US)

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WO WO 2007149096 12/2007(73) Assignee: **The Medicinices Company**, Parsippany, NJ (US)

(\* ) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 0 days.

This patent is subject to a terminal disclaimer.

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**C07K 7/64** (2006.01)  
**C07K 1/00** (2006.01)  
**C07K 1/04** (2006.01)  
**C07K 14/00** (2006.01)

(52) **U.S. Cl.** ..... **530/326; 530/324; 530/333; 530/334; 530/335; 514/13**(58) **Field of Classification Search** ..... None  
See application file for complete search history.(56) **References Cited**

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*Primary Examiner*—Cecilia Tsang*Assistant Examiner*—Julie Ha(74) *Attorney, Agent, or Firm*—Frommer Lawrence & Haug LLP; Sandra Kuzmich; Russell A. Garman(57) **ABSTRACT**

Pharmaceutical batch(es) or pharmaceutical formulation(s) comprising bivalirudin as the active ingredient, and a method of preparing the pharmaceutical batch(es) or pharmaceutical formulation(s). The pharmaceutical batch(es) or pharmaceutical formulation(s) may have a maximum impurity level of Asp<sup>9</sup>-bivalirudin that does not exceed about 0.6%. Also, the pharmaceutical batch(es) or pharmaceutical formulation(s) may have a reconstitution time that does not exceed about 42 seconds. The method of preparing the pharmaceutical batch(es) or pharmaceutical formulation(s) may comprise dissolving bivalirudin in a solvent to form a first solution, efficiently mixing a pH-adjusting solution with the first solution to form a second solution in which the pH-adjusting solution may comprise a pH-adjusting solution solvent, and removing the solvent and the pH-adjusting solution solvent from the second solution.

**20 Claims, No Drawings**